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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/291,925	04/14/1999	AVI J. ASHKENAZI	P1055R1	2757

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EXAMINER

ZEMAN, ROBERT A

ART UNIT PAPER NUMBER

1645

DATE MAILED: 11/20/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/291,925

Applicant(s)

ASHKENAZI ET AL.

Examiner

Robert A. Zeman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 July 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 14-22 and 25-46 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 34-46 is/are allowed.
- 6) ☒ Claim(s) 14-22 and 25-33 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 25.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

The amendment and response filed on 7-25-2002 is acknowledged. Claim 24 has been canceled. Claims 15 and 25 have been amended. Claims 14-22 and 25-46 are pending and currently under examination.

Information Disclosure Statement

The information disclosure statement filed on 7-25-2002 is acknowledged. An initialed copy of said document is attached hereto. It should be noted that not all the listed references were available for consideration. Said references will be considered as they become available.

Claim Objections Withdrawn

The objection to claim 24 as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn. Cancellation of said claim has rendered the objection moot.

Claim Rejections Withdrawn

The rejection of claims 34-37 and 39-43 under 35 U.S.C. 103(a) as being unpatentable over Forster et al. (U.S. Patent 5,641,655 – IDS-5) in view of Ashkenazi et al. (PNAS Vol. 88, pages 10535-10539, 1991 – IDS-5) and Rickles et al. (Journal of Biological Chemistry Vol. 263, No. 3 pages 1563-1569, 1988 – IDS-5) is withdrawn. Applicant's arguments have been fully considered and deemed persuasive.

The rejection of claims 34-46 under 35 U.S.C. 103(a) as being unpatentable over Foster et al. (U.S. Patent 5,641,655 – IDS-5) in view of Ashkenazi et al. (PNAS Vol. 88, pages 10535-10539, 1991 – IDS-5) and Berman et al. (Trends in Biotechnology, Vol. 3, No. 2, pages 51-53, 1985 – IDS-5) is withdrawn. Applicant's arguments have been fully considered and deemed persuasive.

Claim Rejections Maintained

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 14-22 and 25-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Foster et al. (U.S. Patent 5,641,655 – IDS-5) in view of Ashkenazi et al. (PNAS Vol. 88,

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pages 10535-10539, 1991 – IDS-5) and Berman et al. (Trends in Biotechnology, Vol. 3, No. 2, pages 51-53, 1985 – IDS-5) for the reasons outlined in the previous Office action in rejecting claims 14 and 16-46.

Applicant argues:

1. The cited references do not disclose all the elements of the claimed invention and there is no motivation to combine the cited references.
2. None of the cited references teach or suggest glycosylation site deletion variants.
3. Foster et al. do not teach or suggest that the use of a t-PA prosequence could enhance secretion of glycosylation site variant glycoproteins, especially glycosylation site deletion variant mutants.
4. The deficiencies of Foster et al. are not remedied by Ashkenazi et al. or Berman et al.
5. Ashkenazi et al. does not describe site deletion variants.
6. Berman et al. does not teach or suggest that glycosylation site deletion variants can and should be made for expression in eukaryotic cells or that such variants would have alterations in secretion from eukaryotic cells.

Applicant's arguments have been fully considered and deemed to be non-persuasive.

As outlined in the previous Office Action, Foster et al. disclose DNA constructs comprising a first DNA segment encoding a secretory peptide (mammalian t-PA) joined to a second DNA segment encoding a heterologous protein (thrombopoietin). The disclosure by Foster et al. differs from the aforementioned claims in that the heterologous protein encoded by the second DNA segment is thrombopoietin, not TNFR-IgG1. Additionally, Foster et al., as noted by Applicant, does not disclose the use of glycosylation site variants as the products of the

second DNA fragments. However, not only do Ashkenazi et al. disclose the sequence for TNFR-IgG1, but also potential asparagine-linked (N-linked) glycosylation sites (see Figure 1 on page 10536). Since, as disclosed by Berman et al., N-linked glycosylation plays a role in the half-life and antigenicity of the glycoprotein, it would have been, contrary to Applicant's assertion to the contrary, obvious for one of ordinary skill in the art to alter the codons for the potential N-linked glycosylation sites in the sequence of TNFR-IgG1 (disclosed by Ashkenazi et al.) and use the resulting sequences as the second DNA segment in the constructs disclosed by Foster et al. One would have been motivated to make such "TNFR-IgG1 glycosylation variants" in order to, not only take advantage of the increased secretion rates associated with the t-PA pro chimeras disclosed by Foster et al., but to allow for the rapid development of recombinant TNFR-IgG1 proteins with tailored solubility, half-life and antigenic properties.

With regard to Applicant's assertion that Berman et al. does not teach or suggest that glycosylation site deletion variants can and should be made for expression in eukaryotic cells or that such variants would have alterations in secretion from eukaryotic cells: only claim 33 recites said limitation. Additionally, the system of Foster et al. discloses the expression of their constructs in eukaryotic cells.

Conclusion

Claims 14-22 and 25-33 are rejected.

Claims 34-46 are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (703) 608-7991. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703) 308-3909. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

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LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Robert A. Zeman
November 18, 2002